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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	PAPER NUMBER
1648	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,677	PAUZA ET AL.	
	Examiner	Art Unit	
	LOUISE HUMPHREY	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-16,22-28,32,37 and 40* is/are pending in the application.

4a) Of the above claim(s) *12-16,22-28,32,37 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the amendment filed 21 November 2008. Claims 1, 2, 17-21, 29-31, 33-36, 38, 39 and 41-45 have been cancelled. Claims 3-16, 22-28, 32, 37, and 40 are pending. Claims 12-16, 22-28, 32, 37 and 40 are drawn to a nonelected subject matter and hence are withdrawn from further consideration pursuant to 37 CFR 1.142(b). Claims 3-11 are currently examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 3-7 under 35 U.S.C. §112, second paragraph, as being indefinite is withdrawn in response to the Applicants' amendment to the claims.

The rejection of claims 8-11 under 35 U.S.C. §112, second paragraph, as being indefinite is maintained.

Claim 8 recites the "from about 15 to about 21 amino acid residues from the amino terminus region of HIV Tat," which is vague and indefinite because the precise amino acids in question are not readily apparent. Due to the error-prone replication of HIV, there are many quasi species with different amino acid sequences. Especially

when insertion or deletion mutations occur during viral replication, the sequences of the quasi species differ substantially from one another that a skilled artisan would not know whether one position number in one strain is referring to the same position in another strain. Therefore, position numbers in the absence of a reference consensus sequence is vague and indefinite. Applicants may amend the claim language to recite a specific reference amino acid sequence to avoid any further confusion or ambiguity. The phrase "from about 15 to about 21 amino acid residues from the amino terminus region of HIV Tat" does not clarify the recitation "wherein the amino acid sequence comprises at least amino acid residues 1, 7 and 12" in the claim language.

Response to Arguments

Applicants argue that it is clear from both the claim language and the specification that the claimed vaccine comprises a peptide of about 15-21 amino acids in length, where the peptide contains all of amino acid residues 1, 7 and 12 from the amino-terminal end of HIV Tat.

Examiner respectfully disagrees. Applicant's summary of the invention in the remark filed on 21 November 2008 on page 7, as stated above, differs significantly from the claim language: the instant claims recite "amino acid residues 1, 7 and 12" not "amino acid residues 1, 7 and 12 from the amino-terminal end of HIV Tat." The specification (paragraph [0017]) states the invention as "a therapeutic vaccine comprising at least one peptide having at least 15 amino acid residues from the amino terminus region of Tat, wherein the amino acid sequence comprises at least amino acid residue 1, 7 and 12 of the amino terminus of Tat." Without a reference Tat sequence

and the phrase "from the amino terminus of Tat" after the recitation "comprises at least amino acid residues 1, 7 and 12," Applicants have not set the metes and bounds of the claimed invention. The claimed Tat linear epitope peptide is indefinite for reasons as indicated above. Applicants have not responded to the question of whether the claimed invention encompasses all the variable Tat protein sequences as a result of HIV mutation. Neither have Applicants provided any reason why the instant invention does not require a reference Tat protein sequence to define the invention.

The rejection of claim 3 under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement is withdrawn in response to Applicants' amendment.

The rejection of claims 8-11 under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement is maintained.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 I[1, the courts have put forth a series of factors (MPEP §2164.01(a)). See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it

is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

The nature of the invention in claims 8-11 is a broadly claimed HIV vaccine composition comprising about 15 to 21 amino acid residues from the amino terminus of the HIV Tat protein, but the specification does not sufficiently support the full scope of the claimed vaccine. The breadth of the claimed invention is exceedingly large and encompasses a vaccine against any HIV strain.

The state of the art is that the term "vaccine", by definition, implies a preparation intended for active immunological prophylaxis. It should also be able to stimulate high titers of neutralizing antibodies. For example, the Illustrated Dictionary of Immunology defines vaccine as a composition that stimulates protective antibodies and T cell immunity and induces active immunity: "A vaccine should stimulate a sufficient number of memory T and B lymphocytes to yield effector T cells and antibody-producing B cells from memory cells. Injection of a vaccine into a non-immune subject induces active immunity against the modified pathogens"(page 613). "Prophylaxis" is defined as the prevention of disease or of a process that can lead to disease. Although nearly any protein when inoculated can cause an immune reaction, the prophylactic nature of this reaction is not guaranteed and has to be experimentally determined. Given the teachings in the art, it is clear that a compound that merely induces an immune response is not sufficient but must be protective to qualify as a vaccine.

The disclosure fails to provide any working embodiments that meet the claimed limitations. The examples of induction of antibodies by Tat toxoid immunization merely

suggests that the amino-terminal 20 amino acids of Tat protein contain immunogenic epitopes, which is far from a validation or prediction of vaccine efficacy. While there is one example of anti-Tat monoclonal antibody TR1 (against amino acid 1 to 15) and purified IgG from immunized macaques (specification, page 38) neutralizing the transactivation activity of Tat protein in cell culture of $CD4^+$ HeLa cells containing a defective provirus, there are no examples of protection against or prevention from the infection of all strains of HIV in an environment that resembles the natural cause of HIV replication/infection. Furthermore, no *in vivo* working example of any challenge studies is disclosed in the specification.

The specification provides little guidance regarding the making and/or using of the claimed vaccine. The specification does not disclose the protective effect, if any, of expressing or delivering the recited Tat peptide in a diseased or uninfected individual. The amount of direction is limited to the generation of natural immune response in rhesus macaques. However, the immune response to Tat-peptide-inoculate is not predictive of the response to all the HIV strains that the vaccinated subject will contract. Besides, there is no teaching of the type and duration of the immune response. Furthermore, there is no challenge study that measures the T cell count and viral load of the test animals before and after a viral challenge. *In vitro* testing is, at most, useful tool for screening potential anti-viral agents but is not predictive of in vivo effectiveness. *Ex parte Balzarini* (BdPat App&Int) 21 USPQ2d 1892. One skilled in the art would not associate successful *in vitro* testing results with successful *in vivo* AIDS treatment due to the high level of unpredictability of this art.

The art of HIV vaccine is highly unpredictable, since HIV replicates rapidly with a high mutational frequency and creates diverse 'quasi-species', which are favored by the Darwinian selective pressures. Therefore, efforts to develop effective treatments and vaccines must overcome the complex evolutionary dynamics in HIV-infected individuals and within affected populations. The consensus seems to be that induction of both humoral and cellular immunity by an HIV-1 vaccine will be required to achieve maximum protection (Tonini, 2005). It is unclear whether there is any CTL response other than neutralizing antibody response. Importantly, two completed efficacy trials conducted by VaxGen using monomeric HIV-1 envelopes resulted in no clear neutralizing responses against relevant primary HIV strains and no protection against infection (Tonini, 2005). Most importantly, macaque models are not considered adequate working models for humans due to unpredictability (Haigwood, 2004) and hence there cannot be direct extrapolation from macaques to humans without clinical evaluation. Still further, it appears highly unlikely that a single construct will protect against all subtypes of HIV-1 (Tonini, 2005). Even when the vaccine strain matches the challenge strain exactly, the HIV protein delivered by plasmid vectors in the immunization failed to protect the monkeys (Desrosiers, 2004). Therefore, the disclosure does not correlate with protection against any strain and/or clade of HIV, especially when the subject may be a person.

Experimental HIV-1 infection *in vivo* and *in vitro* both suffer from the limitation that the in vitro amplification of HIV-1, which is required to prepare virus stocks for in vitro or in vivo infectivity experiments, impose a genetic selection that results in a

spectrum of variants present in the clinical specimens used to establish the culture (Kusumi, 1992; Meyerhans, 1989). Because of these uncertainties, and even greater uncertainties related to the amount of virus transmitted, the site and cell type involved in initial replication, and the kinetics of virus dissemination, the ability of currently available in vitro or in vivo assays to reliably predict vaccine efficacy is questionable. Small trials in populations with low rates of infection and minimally sized placebo control groups do not have sufficient statistical power to confirm or refute vaccine efficacy.

It is well known in the art that retroviral infections in general, and HIV infections in particular, are refractory to anti-viral therapies. The obstacles to therapy of HIV are well documented in the literature. These obstacles include: 1) the extensive genomic diversity and mutation rate associated with the HIV retrovirus, particularly with respect to the gene encoding the envelope protein; 2) the fact that the modes of viral transmission include both virus-infected mononuclear cells, which pass the infecting virus to other cells in a covert manner, as well as via free virus transmission; 3) the existence of a latent form of the virus; 4) the ability of the virus to evade immune responses in the central nervous system due to the blood-brain barrier; and 5) the complexity and variation of the pathology of HIV infection in different individuals. The existence of these obstacles establish that the contemporary knowledge in the art would not allow one skilled in the art to use the claimed invention with a reasonable expectation of success and without undue experimentation, despite the high level of skill in the art. Further, it is well known in the art that individuals infected with HIV produce

neutralizing antibodies to the virus, yet these antibodies are not protective and do not prevent the infection from progressing to its lethal conclusion.

The complexities of HIV-1 pathogenesis, the high mutation rate of the viral genome, and its ability to persist in lymphoid and other tissues allow HIV-1 to evade many therapies (Yee, 2001). The immune correlates of viral control in the natural history of HIV disease are unclear and, consequently, the required immune responses to therapeutic vaccination remain elusive (Puls, 2006). A natural immune response, consisting of Tat-epitope-specific antibody response as measured in the instant application, is not effective because HIV has evolved a number of evasion strategies: selection for genetic variants that are antigenic escapes variants; inherent resistance to antibody-mediated neutralization; down regulation of major histocompatibility class I molecules from the surface of infected cells by Nef; and destruction of viral-specific $CD4^+$ T helper cells. The main problem with HIV vaccines is that there has not been a solution to overcome the enormous sequence heterogeneity of HIV-1 (see Desrosiers, 2004).

Applicant's specification does not address these factors and does not disclose that the instant invention has overcome these problems. Further, clinical trials using a variety of approaches to vaccinate against HIV-1 have not yielded successful results in the treatment and/or prevention of HIV infection. Thus, it is clear, from the state of the art as evidenced by the published literature and the complete lack of working examples in the instant specification, that treating and/or preventing HIV infection by means of

vaccines is highly unpredictable and has very little success. Therefore, the quantity of experimentation necessary would be excessive and an undue burden on the artisan.

Applicants have not provided sufficient guidance to allow one skilled in the art to make and use the claimed invention with a reasonable expectation of success and without undue experimentation. A therapeutic HIV vaccine comprising a recombinant Tat peptide is not routine in the art, and rather, is considered as problematic and challenging for development. Without sufficient guidance to elicit therapeutic protection against HIV, the experimentation left to those skilled in the art is undue or unreasonable under the circumstances. While Applicant is not required to set forth working examples, the specification must set forth sufficient teachings to allow one to make and use the claimed invention. There is no evidence that the claimed peptides will actually be suitable for vaccinating against HIV. Thus, the instant specification, based on the evidence as a whole, in light of the factors articulated by the court in *In re Wands*, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive. Applicants argue that the prophylactic nature of the administration reaction is demonstrated in both the detection of antibodies generated against Tat and a showing of blocked uptake and transactivation of Tat.

The submitted experimental data in the working example was not convincing for the following reasons: (1) the Tat uptake study is conducted *in vitro* in Jurkat cells, which cannot reflect the entire biological systems in a subject body; (2) elicitation of antibodies in rhesus monkeys are not predictive of therapeutic and protective effects in human bodies, the natural host of HIV, given the lack of correlation in immune responses and therapeutic effects between monkeys and humans (Haigwood, 2004); (3) there is no showing of either decreased viral load or RNA or increased amount of T cells after the administration of the claimed Tat peptide composition; and (3) the differences between experimental inoculation of animals and natural transmission in humans also need to be considered. Since HIV-1 infection in humans results in a wide spectrum of responses and outcomes, it is doubtful any single model will adequately recapitulate such complexity. In conclusion, the disclosure fails to provide any working embodiments that meet the claimed limitation of "therapeutic vaccine."

Furthermore, there is no control for confounding factors such as serum sequestration, bioavailability, a change in the activity just as a matter of time or disease progression, and an effect of other therapies that the infected subjects where exposed to before or during the time course of the experiment. More importantly, Applicants have not responded to the concerns raised against a natural immune response, consisting of Tat-epitope-specific antibody response as measured in the instant application, with respect to a number of evasion strategies employed by HIV through mutational evolution: selection for genetic variants that are antigenic escapes variants; inherent resistance to antibody-mediated neutralization; down regulation of major

histocompatibility class I molecules from the surface of infected cells by Nef; and destruction of viral-specific $CD4^+$ T helper cells.

The amount of antibodies or cytotoxic T cell lymphocytes was not measured in the disclosure or working example. There is no evidence showing the specificity, type, and duration of the claimed protective immune response. Even if the specification discloses a presumptuous viral RNA decrease in rhesus macaques, the inoculate and challenge SIV strain is not predictive of the circulating HIV strains that the vaccinated subject will contract, and the T cell count and viral load of the test animals after challenge are not predictive of the T cell count and viral load of HIV infection at 12, 24, 36 months or even longer after the immunization. There cannot be direct extrapolation from macaques to humans without clinical evaluation (Haigwood, 2004).

The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). See M.P.E.P. §2164.03 [R-2]. Relationship of Predictability of the Art and the Enablement Requirement. In the instant case, there is a high level of unpredictability in the art of HIV peptide vaccine. The immune correlates of viral control in the natural history of HIV disease are unclear and, consequently, the required immune responses to therapeutic vaccination remain elusive (Puls, 2006). In summary, the working example as presented in the specification has not been validated in any animal models or in clinic, and thus, cannot be extrapolated to success in therapeutic vaccinations in any subject against any strain of HIV. Applicants never addressed the issues of discordance

between in vitro studies and human trials. Applicants have not responded to the reasoning and evidence, as indicated on pages 7-11 of the Office Action mailed on 21 May 2008, that demonstrate the unpredictability stemmed from the lack of correlation between *in vitro* data and clinical studies.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 3-7 under 35 U.S.C. §103(a) as being obvious over Frankel *et al.* (US 5,652,122, 29 July 1997, hereinafter "Frankel") is **maintained**.

Claim 3 is drawn to a therapeutic composition comprising at least one peptide having an amino acid sequence consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5 or SEQ ID NO:6. Claims 4-6 further limit the composition to the peptide conjugated to a HIV carrier protein. Claim 7 further limits the composition to comprise a pharmaceutically acceptable carrier.

Although Frankel does not expressly teach a composition comprising HIV Tat, Frankel discloses a composition comprising a pharmaceutically acceptable carrier and a molecule of interest-Tat protein conjugate. The molecule of interest can be an antigen from the bacteria or virus or other infectious agent that the vaccine is to immunize

against (e.g. gp120 of HIV) (column 10, line 57-66). The Tat protein, acting as a transport polypeptide, can be a variant consisting of Tat amino acids (aa) 1-21 fused directly to Tat amino acids 38-72 (column 10, line 13-15; column 40, line 45-47). According to the sequence listed in column 57-58 (SEQ ID NO:7), the Tat amino acids 1-21 match the instantly claimed SEQ ID NO:1 and SEQ ID NO:5. The transport peptides may be advantageously attached to cargo molecules by chemical cross-linking or by genetic fusion (column 3, line 52-54).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the Tat aal-21 peptide with the HIV Env protein, gp120, in a composition as suggested by Frankel *et al.* The skilled artisan would have been motivated to transport any cargo polypeptide, such as HIV Env gp120, by conjugating the cargo with the aal-21 Tat peptide, so as to avoid the problems of spurious trans-activation and disulfide aggregation, while the reduced size of the Tat peptide, as compared to the full size Tat protein, minimizes interference with the biological activity of the cargo molecules (abstract). Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments have been fully considered but are not persuasive. In response to Applicant's argument that one of skill in the art would not use the description of Frankel to generate the claimed therapeutic compositions, as the Tat

fragments in Frankel are used to mediate entry of other proteins into a cell whereas the present invention provides a therapeutic composition that blocks Tat uptake and transactivation, the fact that applicant has recognized another advantage, *i.e.* blocking Tat uptake and transactivation, which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Frankel's disclosed advantage of using Tat peptide to mediate entry of other proteins like Env into a cell is irrelevant and does not distinguish the disclosed composition of Tat-Env conjugate from the instantly claimed composition of Tat-Env conjugate. "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1251, 1254, 195 USPQ 430, 433 (CCPA 1977). See M.P.E.P. §2112 [R-3] I. In other words, Applicant's contention of the function of blocking Tat uptake and transactivation does not impart structural limitations on the claimed invention. The claimed invention is a composition comprising at least one peptide having HIV Tat peptide conjugated to viral Gag, Env, Nef, or fragments thereof. The words "comprising" and "having" are open language that encompass all peptides containing the sequence of SEQ ID NO:1-6. Frankel's peptide composition comprising at least one peptide having SEQ ID NO:1 or SEQ ID NO:5.

Frankel also expressly suggests conjugating a HIV Tat peptide, comprising residues 1-21, with a Env protein, which meets every claim limitation in the instant invention.

Applicant relies on another extraneous fact in the Frankel patent to assert that Frankel teaches away from the instant invention of a peptide consisting only of amino acids 1-21. First, the claimed invention is not limited to consisting only of amino acids 1-21. The open language "comprising..." and "having..." preceding the phrase "selected from a group consisting of" render the claim language open, which reads on any peptides comprising Tat residues 1-21 and any other amino acid sequences. Secondly, even though Frankel discloses that the amino acid sequence preceding the cysteine-rich region of the Tat protein is not required for cellular uptake, Frankel explicitly suggests conjugating Env protein with the fusion protein of Tat residues 1-21 with residues 38-72.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/L. H./
Examiner, Art Unit 1648

/Jeffrey S. Parkin/
Primary Examiner, Art Unit 1648

18 February 2009